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EXAMINER
ROOKE, AGNES BEATA

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/604,779	EWERT ET AL.	
	Examiner	Art Unit	
	Agnes B. Rooke	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-20,23-26 and 33-65* is/are pending in the application.

4a) Of the above claim(s) *51--63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-16,18-20,23-26,33-46,50,64 and 65* is/are rejected.

7)☒ Claim(s) *4-6,17 and 47-49* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____is/ are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This non-final office action is in response to the paper filed on 10/22/2007.

Status of Claims

Claims 1, 4-20, 23-26, 33-50 were previously under examination.

New claims 51-65 were added.

Claims 51-63 are in reference to a distinct invention and would have been restricted if upon original presentation.

Claims 64 and 65 are new and are included in this instant examination because they depend from previously examined claims.

Claims 51-63 are not examined and are thus withdrawn from further examination.

Therefore, claims 1-50, and 64-65 are examination.

Rejections Withdrawn

1. The pervious rejections to claims under 34 USV 112, second paragraph, are withdrawn in view of the amendments to the claims.

2. The previous rejections to claims under 35 USC 102(b) are withdrawn in view of the amendments to the claims.

Objections to Claims

Claims 1-20, 23-26, 33-50, 64, and 65 are objected to because of the following informalities:

Claims 1-20, 23-26, 33-50, 64, and 65 have inconsistencies in naming of chemical compounds or enzymes. Some of the claims use capital letters to designate the names of chemical compounds and enzyme and other claims use small letters to designate the same compounds. Thus, there is not consistency or uniformity of naming they compounds. Thus, proper correction is required.

Objections to Specification

The specification is objected to because of the following informalities:

(a) Specification disclosure is objected to because of the inconsistencies in naming of chemical compounds or enzymes. In the specification, Applicants use capital letters and small letters to name the same chemical compounds (acids, buffers, metals) or enzyme in the text. Thus, there is no consistency in naming. Thus, proper correction is required.

(b) The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.

(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

In the instant application there are subtitles missing regarding: Brief Description of the Drawings or Examples. Therefore, proper correction is required.

(c) The specification is incomplete because the pages of the specification are not numbered.

(d) The last paragraph of the specification ends in the middle of the sentence, and thus the specification seems to be incomplete.

(e) The specification has a font that is distinctly larger than necessary.

(f) The specification should be proof-read for misspelled words (see [0026] for example).

(g) The specification is objected to because trademarks are disclosed throughout the instant specification. The trademark (such as Triton X-100) should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks

should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 11-20, 23-26, 33-43, and 64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite, because the preamble refers to a method of concentrating, detecting and extracting particles from a whole blood but the claimed methods that follows do not list or itemize how the method accomplishes the concentrating or detecting or extracting the particles from a whole blood sample. Therefore, the method is incomplete.

Further, it is indefinite, what consists of the "particles" that are extracted from the method claimed. Therefore, the claim is indefinite.

In addition, the phrase: “coincident relation” in claim 1 is indefinite since the phrase is only used once on page 7 of the specification but does not define what it means. Thus, further specification in the claims is required.

Claim 11 is indefinite because of its phrase “separate and dried state.” In claim it states that plasminogen and streptokinase are frozen together, and claim 11 refers to

plasminogen and streptokinase in a dried state. Therefore, the claim 11 is indefinite and lacks antecedent basis to claim 1, since frozen does not necessarily mean dry.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-6, 8-20, 23-50, 64, and 65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In claim 1, Applicants refer to concentrating, detecting and extracting any "particles" from a whole blood where the particles are not disclosed in the claim as currently presented. Therefore, the claim is overly broad because it encompasses genus of any particles (chemical compounds such as inorganic compounds or organic compounds or any fragments of peptides, for example). Therefore, the structure of the particles do not correspond to their function, since those particles can be presented by any chemical structure or by any small fragments or variants of peptides, for example. Therefore, the written description is not satisfied.

Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991), states that "applicant must convey with reasonable clarity to those

skilled in the art that, as of the filing date sought, he or she was in *possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. *See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993).*

Therefore, because the genus of any particles is so broad and no examples of such compounds or structures are presented in the claims, the written description is not satisfied because there is no nexus between the structure of a particle and its function.

New matter Rejection

Claims 11-20, 23-26, 33-43, and 64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In claim 11, the phrase "**separate** and dried state" does not have support in the specification and thus constitutes a new matter. All dependent claims 12-20, 23-26, 33-43, and 64 are included in this rejection because they depend from base claim 11.

If to the contrary, Applicants are required to point out where such support is presented in the specification.

Rejections Maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 7, 9-12, 16, 18, 19, 31, 33, 44-46, 50, 64, and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson et al. (J. Clin. Microbiol, 1978) in view of Dupe et al. (thrombosis and Haemostas, 1981).

Watson et al. teach a method of trapping bacteria from blood sample in a clot, then digesting the clot buy adding streptokinase, and culturing the bacteria for identification; where they add this blood to a medium containing sodium tauerochlorate which is a bile surfactant, reading on a detergent, and which also contains 100 U streptokinase,(see page 123, column 2, to page 124, column 1). The method used in Watson is congruent with the procedure described in the specification (see [0045] and [0046]). Regarding the limitation that the sample is exposed to plasminogen, the whole

blood sample must be inherently exposed to plasminogen because blood is known to contain plasminogen, and streptokinase would not dissolve clots without activating downstream plasminogen.

Watson et al. do not expressly teach maintaining plasminogen and streptokinase in a frozen state, or that the solution comprise NaCl, or that the streptokinase/plasminogen should be kept in a dried state, or that the plasminogen and streptokinase are resuspended in a buffer solution and added to blood and incubated at room temperature, or that the mixture should be centrifuged, the supernatant decanted, and the pellet washed.

Dupe et al. teach a method of assaying thrombus dissolution by streptokinase/plasminogen complexes in whole blood; where the streptokinase and plasminogen can be prepared ahead of time; where plasminogen and streptokinase were both available in a pharmaceutical grade lyophilized powder (see pages 530-531). The companies that provide the composition mixed them and ship them in containers (see page 530) (Regarding the limitations recited in claims 18 and 19, practice of separating clots from serum by centrifugation ha been well established in the art of clinical hematology for decades.

Claims 50, 64 and 65 are included in this rejection because the enzyme-detergent combination can comprises an enzyme that can break down a nuclear membrane (claim 64) and the method can be conducted at pH 7.8 that is close to the normal pH of blood that is pH of 7.4 (claim 65).

A person of ordinary skill in the art at the time the invention was made would have been motivated to prepare streptokinase and plasminogen in either a frozen or lyophilized form because Dupe et al. teach that they can be stored fro longer periods of time preserved in such manner, and Watson et al. teach that streptokinase is useful reagent for isolating bacteria from blood cultures.

Hence, it would have been prima facie obvious tone of ordinary skill in the art at the time the invention was made to freeze or lyophilize streptokinase and plasminogen to store for later use in a method of isolating bacteria.

Claims 1, 7, 9, 10-12, and 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson (J Clin Microbiol, 1978) in view of Smith et al (Thromb Haemostas, 1982).

The teachings of Watson are discussed above and applied as before.

Watson et al do not expressly teach that enzymes are freeze dried for storage.

Smith et al teach that plasminogen and streptokinase can be separately purified and lyophilized in individual containers for long-term storage (see "Fibrinolytic agents", p. 269, col. 2, for example).

A person of ordinary skill in the art at the time the invention was made would have been motivated to lyophilize plasminogen and streptokinase because Smith et al teach that these enzymes retain activity when preserved in this manner, and preservation allows for long-term storage of useful reagents.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to lyophilize streptokinase and plasminogen in preparation for isolating bacteria from blood in the method of Watson.

Claims 1, 7, 9, 10, and 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson (J Clin Microbiol, 1978) in view of Cassels et al (Thromb Haemostas, 1982).

The teachings of Watson are discussed above and applied as before.

Watson does not expressly teach the use of phosphate in a storage solution. Cassells et al teach that phosphate is a suitable medium for carrying out reactions comprising plasminogen and streptokinase (see "Clot-lysis assay, p. 396, col. 2, for example). Additionally it is standard practice in the art of protein purification to snap-freeze proteins in phosphate-buffered saline, for example for storage.

A person of ordinary skill in the art at the time the invention was made would have been motivated to freeze streptokinase in a phosphate buffer because Cassels et al teach that a phosphate buffer is compatible with streptokinase activity, and it is well-known in the art to freeze proteins in a phosphate buffer such as PBS, for example.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to freeze streptokinase in a phosphate buffer.

Claims 1, 7, 9-16, 18, 19, 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson et al. in view of Dupe et al. and further in view of Kreilgaard et al. (1998).

The teachings of Watson and Dupe are disclosed above where they do not expressly teach the lyophilization of streptokinase or plasminogen in trehalose.

Kreilgaard et al. teach that trehalose can be added to a protein before freeze drying process and that trehalose affords protection to enzymes during freeze drying and storage as dried silid (see page 121, column 2, fro example).

It would have been obvious to one of ordinary skilled in eth art at eth time the invention was made to include trehalose in a method of freeze drying an enzymatic combination taught by Dupe et al. because Dupe et al. teach that it is possible to freeze dry enzyme in separate vials and Kreilgaad et al. teach that trehalose is useful sugar to add to an enzyme composition before freeze-drying. One would be motivated to do so for the expected benefit of protection of particles.

Claims 1, 2, 7-11, 16, 18, 19, 23-26, 33, 34, 44-46, 49 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson (1978) in view of Zhang et al (1995) in view of Dupe et al (1981), in view of Zierdt et al (1977) and in view of Hallick et al (Nucleic Acid Res, 1977).

The teachings of Watson (1978), Zhang et al (1995) and Dupe et al (1981) are discussed above and applied as before.

Additionally, Zhang et al teach that blood samples can be lysed using glass beads and vortexing, and then centrifuged to remove gross blood byproducts before the supernatant is decanted and processing continued with a Qiagen blood mini amp kit (see Materials and Methods, p. 597, for example). The Qiagen blood mini amp kit teaches the use of proteinase K and SDS as components of the process of purifying DNA from blood samples (see Qiagen DNA blood mini kit handbook, p. 12, for example). Also as discussed above, Zhang et al teach the use of citrate as an anticoagulant.

None of the above references expressly teaches the use of endonuclease inactivation, DNAse inactivation, or addition of aurintricarboxylic acid to the sample.

None of the references teaches the inclusion of octylphenol ethoxylate (Triton X-100).

Hallick et al teach that aurintricarboxylic acid (ATA) is a general nuclease inhibitor (see Introduction, p. 3055, for example). They demonstrate that addition of ATA to a nuclease reaction inhibits the reaction (see Figs 1 and 2, p. 3058, for example). Additionally they suggest that it would be useful to add ATA to prevent degradation of nucleic acids during nucleic acid isolation (see Introduction, p. 3055, for example).

Zierdt et al (1977) teach that Triton X-100 is advantageously added to a blood solution in a method of purifying bacteria present in the blood. The procedure allows one to lyse blood cells without damaging the bacteria (see Materials and Methods, p. 46, col. 2, for example).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add ATA and Triton X-100 when performing the assay of liberating particles, because Zhang et al teach that one can perform PCR from purified bacterial DNA, Zierdt et al teach that one can isolate bacteria from whole blood in a method comprising Triton X-100, and Hallick et al teach that addition of ATA inhibits nucleases and suggest its usefulness when one desires to purify DNA. One would have been motivated to do so for the expected benefit that using ATA and Triton X-100 would provide higher yields of quality DNA.

Based upon the teachings of the cited references, the level of skill of one of ordinary skill in the art, and absent any evidence to the contrary, one would have a reasonable expectation of success in practicing the claimed invention.

Claims 1, 7-11, 16, 18, 19, 23-26, 33, 34, 39, 44-46, 49, 50, 64, and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson (1978) in view of Zhang et al (1995) in view of Dupe et al (1981) in view of Hallick et al (Nucleic Acid Res, 1977) and in view of Zierdt (J Clin Microbiol, 1982).

This is a new rejection.

The teachings of Watson (1978), Zhang et al (1995) Dupe et al (1981) and Hallick et al (1977) are discussed above and applied as before.

None of the references expressly teaches the use of 10 mM potassium phosphate.

Zierdt teaches that the buffer should contain 10 mM sodium phosphate (see p. 172, col. 2, for example).

A person of ordinary skill in the art at the time the invention was made would have been motivated to use potassium phosphate in a method of isolating bacteria because Zierdt teaches that a 10 mM sodium phosphate buffer is suitable in a method of isolating bacteria from blood, and potassium phosphate is a suitable equivalent.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a 10 mM potassium phosphate buffer in a method of isolating bacteria from blood.

Applicants Responses

Applicants responded and stated that just because they amended claim 1 to include limitations from claims 2 and 3, thus the rejection should be dropped.

Examiner maintains the rejections as presented above because they address the limitations pf eth claims as presented above. Further, the lyophilization of streptokinase and plasminogen is widely used in the art and is available from commercial vendors and expressly described by the cited references.

Objections to Claims

Claims 4-6, 17, and 47-49 are objected to because they depend from rejected base claim.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnes B. Rooke whose telephone number is (571)272-5358. The examiner can normally be reached on MAX/FLEX

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on (571)272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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